

REMARKS

Claims 14, 15, 17-24, 34-38, 40-43, 49-51, 55-65, and 67-69 are pending. Claims 16, 39, 52-54, and 66 have been canceled herein. Claims 14, 23, 34, 49, 50, and 51 have been amended herein. Support for these amendments can be found throughout the specification and originally filed claims. Thus, no new matter has been added.

Rejection under 35 U.S.C. §102

Claims 14-16, 24, 34-39, 49-50, 55-57, and 65-67 were rejected under 35 U.S.C. §102(b) as anticipated by Hata *et al.* (U.S. patent number 4,871,539). The Examiner states that Hata discloses a method of using a probiotic composition with *Bacillus* species including *Bacillus coagulans* and *Bacillus subtilis* topically to pubic and vaginal areas. (See Office Action at page 6).

Claims 16, 39, and 66 have been canceled. Thus, this rejection, as it applies to these claims, is moot and should be withdrawn. Pending independent claims 14, 34 and 49 have been amended herein to specify a composition comprising a bacterial component consisting of *Bacillus coagulans* Hammer (ATCC# 31284) bacteria. According to the MPEP, “The traditional phrase ‘consisting of’ excludes any element, step, or ingredient not specified in the claim.” (See MPEP § 2111.03.) Thus, claims 14, 34 and 49, as currently amended, exclude bacterial strains other than *Bacillus coagulans* Hammer (ATCC# 31284). Hata does teach the use of *Bacillus coagulans* Hammer (ATCC# 31284) as required by amended claims 14, 34 and 49.

For these reasons, Applicants therefore request withdrawal of this rejection.

Rejection under 35 U.S.C. §103

Claims 14-16, 20-22, 24, 34-39, 41-43, 49-50, 55-57, and 59-67 were rejected under 35 U.S.C. §103(a) as unpatentable over Hata in view of Gibson *et al.* (Gastroenterology (1995) 109:975) and Japanese patent application JP 3-192200. Claims 16, 39, and 66 were canceled. Thus, this rejection, as it applies to these claims, is moot and should be withdrawn. The Examiner states that Hata does not disclose the use of sugars such as FOS and additional bath oils, salts, and surfactants, but that Gibson teaches that the addition of FOS stimulates probiotic bacteria that contact a mucous membrane, and that JP 3-192200 teaches the addition of salts and

surfactants into detergent compositions with *Bacillus coagulans* and *Bacillus subtilis*. (See Office Action at pages 7-8.)

Pending claims 14, 15, 20-22, 24, 34-38, 41-43, 49-50, 55-57, 59-65, and 67 as currently amended, specify *Bacillus coagulans* Hammer (ATCC# 31284). As discussed above, Hata does teach the use of *Bacillus coagulans* Hammer (ATCC# 31284) as required by amended claims 14, 34 and 49. The Hata reference is limited to the use of *Bacillus coagulans* in combination with other bacteria (*Lactobacillus clearans* and, optionally, *Streptococcus faecalis*). Gibson and JP 3-192200 do not cure this deficiency, as neither reference teaches methods of topically applying a probiotic composition containing only *Bacillus coagulans* Hammer (ATCC# 31284) bacteria. Thus, pending claims 14, 15, 20-22, 24, 34-38, 41-43, 49-50, 55-57, 59-65, and 67 are not obvious in view of the combination of Hata, Gibson, and JP 3-192200. This rejection should be withdrawn.

Rejection under 35 U.S.C. §112, first paragraph

Claims 14-24, 34-43, and 49-69 were rejected under 35 U.S.C. §112, first paragraph as not enabled. The Examiner states that the as-filed application does not enable one skilled in the art to practice the invention without an undue amount of experimentation. In applying this rejection, the Examiner has focused upon three of the factors summarized by In re Wands, 858 F.2d 731 (1988), the scope of the claims, the unpredictability of the art, and the amount of experimentation required to enable one skilled in the art to practice the claimed invention. (See, Office action, page 2.) Applicants disagree for the reasons listed below.

The scope of the claims.

The Examiner has indicated that the breath of the claims is directed to a method for inhibiting and treating bacterial, yeast, fungal and/or viral infections including vaginal infections by applying topically to skin or mucous membrane probiotic compositions with *Bacillus* species. (See, Office action at page 3.) The Examiner also states that the specification does not adequately teach how to effectively inhibit all bacterial, yeast, fungal and/or viral infections including vaginal infections because no animal cells or live animals were used. (See, Office action at page 3.) The Examiner further states that the specification only discloses the *in vitro*

assays (example 1, pages 24-27) of antimicrobial activity of one representative of *Bacillus coagulans* such as strain ATCC 31284. (See, Office action at page 3.)

The claims have been amended to address the Examiner's concerns. Independent claim 14 has been amended herein to specify a method of inhibiting yeast or fungal infection by applying topically to skin or a mucous membrane of a mammal a probiotic composition comprising a bacterial component, said bacterial component consisting of *Bacillus coagulans* Hammer (ATCC# 31284). Further, amended claim 14 specifies that the *Bacillus coagulans* bacteria grow topically for sufficient time to inhibit growth of yeast or fungus. Similarly, claim 49 has been amended herein to specify a method of treating a vaginal infection, comprising: identifying a subject suffering from a vaginal infection; and applying topically to the skin or a mucous membrane of said subject a composition comprising a bacterial component consisting of *Bacillus coagulans* Hammer (ATCC# 31284). As noted by the Examiner, the as-filed specification discloses the use of *Bacillus coagulans* Hammer (ATCC# 31284) to inhibit infections of *Trichophyton* species and *Candida* species. (See, e.g., Example 1, pages 24-27.) These data demonstrate the inhibitory effectiveness of the *Bacillus coagulans* Hammer (ATCC# 31284). A zone of inhibition of microbial growth on a plate is a reliable indicator of growth inhibition on another surface, i.e. skin or mucous membrane of a mammal.

The predictability of the art.

The Examiner has indicated that the claimed methods are drawn to generic representatives assigned to the species of *Bacillus coagulans*. (See Office Action at page 4.) The Examiner further states that Sytnik (IDS reference; Mikrobiologicheskii Zhurnal, 1989, 51, 1:82-87) demonstrates that at least some strains of the claimed *Bacillus coagulans* do not inhibit all clinical *Staphylococcus* infections. In response, Applicants note that claim 14 has been amended to recite a method of inhibiting yeast or fungal infection comprising: applying topically to skin or a mucous membrane of a mammal a probiotic composition comprising a bacterial component, said bacterial component consisting of *Bacillus coagulans* Hammer (ATCC# 31284). Thus, the Sytnik reference is not relevant to the claimed invention. As noted by the Examiner, the as-filed specification discloses the use of *Bacillus coagulans* Hammer (ATCC# 31284) to inhibit infections of *Trichophyton* species and *Candida* species. (See, e.g., Example 1, pages 24-27.)

The Examiner has also indicated that the art provides no reasonable expectation of success for claims drawn to inhibiting various topical and mucous membrane infections including vaginal infection, citing a passage by Seligman (British J. of Obstetrics and Gynaecology, 1995, 102:763-64), which states that studies of the use of *Lactobacilli* in the treatment of vaginitis and vaginosis have almost all been limited, uncontrolled, and have given variable results. (Seligman at page 763, paragraph 4.) In response, Applicants note that, Seligman also cites a study in which the use of *L. acidophilus* successfully controlled candidal vaginitis (Hilton *et al.* Annals Int. Med. 116:353-57, 1992). Thus, contrary to the Examiner's assertion, the state of the art provides a reasonable expectation of success.

Further, claim 50 has been amended to recite a method of treating a vaginal infection, comprising: identifying a subject suffering from a vaginal infection; and applying topically to the skin or a mucous membrane of said subject a composition comprising a bacterial component consisting of *Bacillus coagulans* Hammer (ATCC# 31284), wherein said infection is caused by a yeast pathogen. As described above, the as-filed specification discloses the use of *Bacillus coagulans* Hammer (ATCC# 31284) to inhibit infections of *Trichophyton* species and *Candida* species. (See, e.g., Example 1, pages 24-27.) These data confirm the predictability of the claimed methods using an experimental system that is well-recognized in the art - zones of inhibition of microbial growth on culture plates.

According to the Examiner, Seligman also teaches that the ability of bacteria to adhere to animal epithelial cells is an important factor in colonization of mucous membrane or vagina and that different species show varying effects. (See, Office action, page 4.) The Examiner states that the ability of the claimed *Bacillus* species, including ATCC# 31284, to adhere to animal cells is unpredictable and that selection of desirable *Bacillus* species would require undue experimentation. Applicants have amended the claims to require a particular species and strain of *Bacillus*, i.e., *Bacillus coagulans* Hammer (ATCC# 31284). Moreover, the specification discloses that *Bacillus coagulans* strains colonizes tissue, including skin and mucous membrane tissues. (See, e.g., page 7, lines 6-19.) Thus, the claimed methods would not require the selection of a *Bacillus* species or undue experimentation.

The amount of experimentation required.

The Examiner states that the claimed doses and/or protocols for administration are generic considerations and they are not supported for the whole breadth of instant claims because neither claimed doses nor claimed protocols have been demonstrated in models involving animal cells and/or live animals and because the claimed doses have not been demonstrated as effective for colonization of skin or mucous membrane including vagina. (See Office action at page 5.) The Examiner also states that the specification does not teach how to extrapolate data obtained from *in vitro* biological studies to the development of *in vivo* mammalian (e.g., human) treatment. Applicants disagree. The as-filed specification discloses the use of specific concentration of *Bacillus coagulans* bacteria to inhibit the growth of a representative number of pathogens as compared to a positive control treatment of 2% miconazole provided in a similar volume. (See, e.g., Example 1, pages 24-27.) The results described in the specification were obtained with *Bacillus coagulans* Hammer obtained from the American Type Culture Collection (ATCC# 31284). As mentioned previously, claim 14 has been amended to specify *Bacillus coagulans* Hammer (ATCC# 31284).

Not only is one skilled in the art able to use the relative amounts of the *Bacillus coagulans* bacterial composition and the positive control miconazole to extrapolate specific effective dosages for *in vivo* treatment of humans and other mammals, the specification in numerous places (e.g., page 27, lines 16, 23 and 30; page 28, line 8; page 30, line 9 to page 31, line 5; page 31, line 12 to page 32, line 3; page 32, lines 4-14; page 32, line 23 to page 33, line 2; page 33, lines 15-22; page 34, lines 6-12; page 35, lines 21-27; page 36, lines 8-11 and 15-18; and page 37, lines 8-9) provides specific ranges or absolute amounts of bacteria or spores to be used in the claimed methods. For this reason, an ordinary practitioner would have no difficulty carrying out the claimed methods.

For the above-stated reasons, Applicants assert that the methods as presently claimed are predictable and that the level of experimentation left to the skilled practitioner is not unnecessary, improper, extensive, or undue. Therefore, the pending claims, as amended herein, are fully enabled, and this rejection should be withdrawn.

CONCLUSION

On the basis of the foregoing amendments and remarks, Applicants respectfully submit that this paper is fully responsive and that the pending claims are in condition for allowance. Such action is respectfully requested. If there are any questions regarding these amendments and remarks, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,



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